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Synthesis of Hindered *t*-Alkyl Ethers

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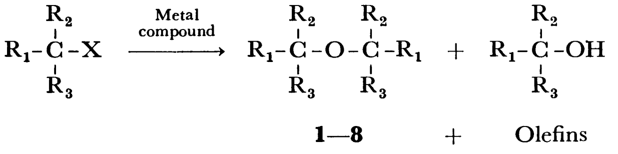
Di-*t*-butyl ether was prepared in 6—73% yields by the reactions of *t*-butyl halide with Ag_2CO_3, Ag_2O, HgO, ZnO, $ZnCO_3$, PbO_2, $Cu_2(CO_3)(OH)_2$, and Tl_2O_3 at 20—65 °C in hydrocarbons under nitrogen. Similar reactions gave seven new hindered di-*t*-alkyl ethers: di-*t*-pentyl ether, bis(1,1-dimethylbutyl) ether, bis(1-ethyl-1-methylpropyl) ether, bis(1,1-dimethylpentyl) ether, bis(1-ethyl-1-methylbutyl) ether, bis(1,1-diethylpropyl) ether, and bis(1,1-dimethylhexyl) ether. The yield of di-*t*-alkyl ether decreased as the *t*-alkyl group became bulky. A slight difference in the skeletal structure of the *t*-alkyl halide markedly influences the substitution. The reaction pathways are elucidated on the basis of the experimental results.

Sterically hindered di-*t*-alkyl ethers have never been prepared by any usual procedure, such as dehydration of alcohols or the Williamson synthesis. Only di-*t*-butyl ether has been obtained by some specific procedures.[1-3)]

This work deals with the syntheses of unknown di-*t*-alkyl ethers by the reactions of *t*-alkyl halides with various metal compounds. Furthermore the reaction pathways and the steric effects of *t*-alkyl groups on their reactivity were investigated in detail.

Results and Discussion

A series of *t*-alkyl halides was allowed to react with various metal compounds in pentane and hexane under optimum conditions. The products were di-*t*-alkyl ether, *t*-alkyl alcohol, and olefins, as illustrated in Scheme 1.



$$R_1\text{-}\underset{R_3}{\overset{R_2}{C}}\text{-}X \xrightarrow[\text{compound}]{\text{Metal}} R_1\text{-}\underset{R_3}{\overset{R_2}{C}}\text{-}O\text{-}\underset{R_3}{\overset{R_2}{C}}\text{-}R_1 + R_1\text{-}\underset{R_3}{\overset{R_2}{C}}\text{-}OH$$

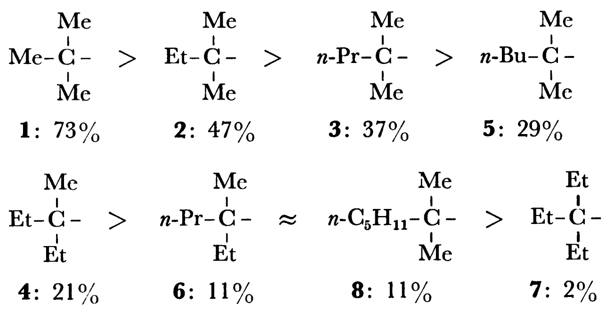
1—**8** + Olefins

1: $R_1=R_2=R_3=Me$ **5**: $R_1=R_2=Me$, $R_3=n\text{-}Bu$
2: $R_1=R_2=Me$, $R_3=Et$ **6**: $R_1=Me$, $R_2=Et$, $R_3=n\text{-}Pr$
3: $R_1=R_2=Me$, $R_3=n\text{-}Pr$ **7**: $R_1=R_2=R_3=Et$
4: $R_1=Me$, $R_2=R_3=Et$ **8**: $R_1=R_2=Me$, $R_3=n\text{-}C_5H_{11}$

Scheme 1.

Table 1 shows the results in detail. The reaction of *t*-butyl chloride with silver carbonate at 20 °C for 20 h gave **1** in 73% yield (Run 1). A similar reaction of silver(I) oxide at 35 °C also gave **1** in 63% yield (Run 2). Mercury(II) oxide reacted more slowly with *t*-butyl and *t*-pentyl chlorides, and 2-chloro-2-methylpentane to give **1**, **2**, and **3** respectively in reasonable yields (Runs 3, 14, and 19). In the case of zinc compounds, **1** and **2** were afforded only on addition of *t*-alkyl alcohol to the system (Runs 4, 5, and 15). This result suggests the participation of the alcohol in the formation of **1** and **2**. Lead(IV) oxide and copper(II) carbonate hydroxide failed to complete the reaction even under certain strict conditions (Runs 6 and 7). Thallium(III) oxide readily reacted with *t*-butyl chloride to give **1**, but in only 6% yield (Run 8). Consequently, silver(I) oxide and carbonate gave better results than the other metal compounds. *t*-Butyl and *t*-pentyl bromides also reacted with two equivalents of silver compound at much lower temperatures than the corresponding chlorides (Runs 9, 10, and 16). Calcium hydride retarded the reaction and decreased markedly the distributions of both *t*-pentyl alcohol and **2** (Run 13).

On the whole, the yield of the ether decreased as the *t*-alkyl group became bulky (Runs 11—27). When one of the methyl groups of *t*-butyl chloride was substituted for ethyl, propyl butyl, and pentyl groups, the yields of **2**, **3**, **5**, and **8** were 47, 37, 29, and 11% respectively. The substitution of methyl groups of the chloride for two or three ethyl groups resulted in a more remarkable decrease: the yields of **4** and **7** were 21 and 2%, respectively. Scheme 2 illustrates the relationship between the structure of the *t*-alkyl group and the yield of di-*t*-alkyl ether.



Scheme 2.

It is interesting from a structural point of view that the yields of isomeric **3** and **4** are quite different (Runs 17 and 20). An analogous tendency is observed in isomeric **5**, **6**, and **7** (Runs 22, 24, and 26). To sum up, the yield is greatly influenced by the degree of bulkiness and the structure of the *t*-alkyl group.

Table 2 shows the time-course of the reaction of *t*-pentyl chloride with a small excess of silver carbonate at 20 °C (*cf.* Run 11). The proportions of the chloride and the products were followed by GLPC at regular time intervals. The initial step of this reaction was so fast that half of the chloride was consumed in a few hours. The proportions of **2** and of the olefins (2-methyl-1-butene and 2-methyl-2-butene) increase with an increase in reaction time, while that of *t*-pentyl alcohol remains almost constant over several hours.

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TABLE 1. REACTIONS OF *t*-ALKYL HALIDES WITH METAL COMPOUNDS

Run	Substrates[a]		Conditions			Yield (%) of products[c]		
	t-Alkyl halide	Metal compound (mmol)	Solvent[b]	Temp °C	Time h	Ether	Alcohol	Olefin
1	*t*-BuCl	$\mathrm{Ag_2CO_3}$	P	20	20	**1**, 73	7	16
2	*t*-BuCl	$\mathrm{Ag_2O}$	P	35	20	**1**, 63	12	21
3	*t*-BuCl	HgO	P	35	20	**1**, 59	24	13
4	*t*-BuCl[d]	ZnO (26)	H	55	20	**1**, 37	—	42
5	*t*-BuCl[d]	$\mathrm{ZnCO_3}$	P	35	20	**1**, 10	—	11
6	*t*-BuCl	$\mathrm{PbO_2}$	H	65	50	**1**, 15	15	48
7	*t*-BuCl	$\mathrm{Cu_2(CO_3)(OH)_2}$	P	35	200	**1**, 12	18	28
8	*t*-BuCl	$\mathrm{Tl_2O_3}$	P	20	6	**1**, 6	49	41
9	*t*-BuBr	$\mathrm{Ag_2CO_3}$ (40)	P	−20	5	**1**, 56	16	24
10	*t*-BuBr	$\mathrm{Ag_2O}$ (40)	P	0	5	**1**, 55	34	7
11	$\mathrm{Et(Me)_2CCl}$	$\mathrm{Ag_2CO_3}$	H	20	20	**2**, 47	21	32
12	$\mathrm{Et(Me)_2CCl}$	$\mathrm{Ag_2O}$	H	35	20	**2**, 34	27	39
13	$\mathrm{Et(Me)_2CCl}$[e]	$\mathrm{Ag_2O}$	H	35	40	**2**, 16	1	83
14	$\mathrm{Et(Me)_2CCl}$	HgO	H	40	40	**2**, 16	30	54
15	$\mathrm{Et(Me)_2CCl}$[f]	ZnO (26)	H	55	13	**2**, 10	—	45
16	$\mathrm{Et(Me)_2CBr}$	$\mathrm{Ag_2CO_3}$ (40)	H	−20	5	**2**, 35	15	50
17	*n*-$\mathrm{Pr(Me)_2CCl}$	$\mathrm{Ag_2CO_3}$	P	20	20	**3**, 37	26	37
18	*n*-$\mathrm{Pr(Me)_2CCl}$	$\mathrm{Ag_2O}$	P	35	20	**3**, 36	24	35
19	*n*-$\mathrm{Pr(Me)_2CCl}$	HgO	P	35	100	**3**, 13	40	45
20	$\mathrm{Me(Et)_2CCl}$	$\mathrm{Ag_2CO_3}$	P	20	20	**4**, 21	37	42
21	$\mathrm{Me(Et)_2CCl}$	$\mathrm{Ag_2O}$	P	35	20	**4**, 10	40	49
22	*n*-$\mathrm{Bu(Me)_2CCl}$	$\mathrm{Ag_2CO_3}$	P	20	20	**5**, 29	30	40
23	*n*-$\mathrm{Bu(Me)_2CCl}$	$\mathrm{Ag_2O}$	P	35	20	**5**, 31	25	40
24	*n*-Pr(Et)(Me)CCl	$\mathrm{Ag_2CO_3}$	P	20	20	**6**, 11	35	54
25	*n*-Pr(Et)(Me)CCl	$\mathrm{Ag_2O}$	P	35	20	**6**, 9	18	66
26	$\mathrm{Et_3CCl}$	$\mathrm{Ag_2CO_3}$	P	20	20	**7**, 2	40	50
27	*n*-$\mathrm{C_5H_{11}(Me)_2CCl}$	$\mathrm{Ag_2CO_3}$	P	20	20	**8**, 11	38	51

a) *t*-Alkyl halide 40 mmol and metal compound 22 mmol used unless otherwise stated. b) Pentane (P) or hexane (H) 20 cm^3 used. c) GLPC yields based on *t*-alkyl halide. d) *t*-Butyl alcohol 40 mmol added. e) Calcium hydride 20 mmol added. f) *t*-Pentyl alcohol 40 mmol added.

This observation suggests that the alcohol is consumed during the reaction. The other *t*-alkyl chloride also gave similar results.

The following pathways therefore are proposed for the reaction of *t*-alkyl halide with silver carbonate:

$$\mathrm{R\text{-}X + Ag_2CO_3 \xrightarrow{E} R'\text{-}C{=}C + AgX + AgOH + CO_2} \qquad (1)$$

$$\mathrm{R\text{-}X + AgOH \longrightarrow R\text{-}OH + AgX} \qquad (2)$$

$$\mathrm{R\text{-}X + R\text{-}OH + Ag_2CO_3 \xrightarrow{S} R\text{-}O\text{-}R + AgX + AgOH + CO_2} \qquad (3)$$

The elimination of *t*-alkyl halide with silver carbonate gives olefins, silver halide, and silver hydroxide (Eq. 1). Silver hydroxide reacts with *t*-alkyl halide to give *t*-alkyl alcohol (Eq. 2). A desiccant such as calcium hydride would partly react with silver hydroxide and suppress the conversion into the alcohol.[4] The desired ether is formed from the halide and the alcohol in the presence of silver carbonate (Eq. 3). As the reaction is carried out in nonpolar solvents, the ether is given by bimolecular nucleophilic substitution. Such pathways can also be estimated for the reactions of the other metal compounds. These equations explain successfully the distribution of the products, the steric hindrance of the *t*-alkyl group, and the additive effect of the alcohol or calcium hydride.

TABLE 2. PROPORTIONS OF *t*-PENTYL CHLORIDE AND ITS PRODUCTS DURING THE REACTION

Time h	Proportions[a] (%)			
	t-$\mathrm{C_5H_{11}Cl}$	**2**	*t*-$\mathrm{C_5H_{11}OH}$	Olefins[b]
0	100	0	0	0
0.5	76	7	7	10
1	68	10	10	12
2	53	18	12	17
3	41	24	14	21
5	27	32	18	23
7	16	37	21	26
10	11	40	21	28
15	5	44	21	30
20	0	47	21	32

a) The proportions were available from the more detailed results on Run 11 in Table 1. b) 2-Methyl-1-butene and 2-methyl-2-butene.

Experimental

Materials. All inorganic chemicals were commercial extra pure or GR grade reagents, dried over silica gel, and used without further purification. 2-Chloro-2-methylpentane, 3-chloro-3-methylpentane, 2-chloro-2-methylhexane, 3-chloro-3-methylhexane, 3-chloro-3-ethylpentane, and 2-chloro-2-methylheptane were derived from the corresponding alcohols.[5–8] Organic chemicals were distilled from calcium hydride before use and their purities were checked by GLPC.

Procedure and Analysis. In a three-necked flask, fitted with a reflux condenser, a dropping funnel, and a magnetic stirrer, 40 mmol of *t*-alkyl halide was added to 22 mmol of metal compound in 20 cm^3 of pentane or hexane medium. The mixture was stirred at a given temperature under nitrogen. The products in the solution were determined by GLPC comparison with authentic samples using toluene, *o*-xylene, and mesitylene as internal standards (Table 1). GLPC analyses were performed on a Shimadzu GC-3AH chromatograph using 3 m×3 mm columns packed with 5% DNDP and 5% Silicone DC 550 on 80—100 mesh Celite support. NMR spectra were determined with a JEOL-PS-100 high resolution spectrometer operating at 100 MHz. Chemical shifts are reported in δ units from internal TMS. IR spectra were recorded on a JASCO DS-301 spectrometer. Mass spectra were recorded on a JEOL JMS-01SG spectrometer with ionization current 75 eV. The molecular weights of some ethers were measured by cryoscopy in benzene.

*Characterization of Di-*t*-alkyl Ethers.* The preparative scale reaction of *t*-alkyl chloride (0.2 mol) with silver carbonate (30.33 g, 0.11 mol) in pentane (100 cm^3) was carried out at 20 °C for 20 h in a manner similar to that above. The reaction mixture was filtered. The filtrate was concentrated and rectified over potassium carbonate, giving di-*t*-alkyl ether (purity >99.5%), which was identified by its physical constants, NMR, IR, and mass spectra.

*Di-*t*-butyl Ether (**1**)*: Yield, 5.60 g (43%); bp 106 °C; IR (neat) 1384, 1363 (*t*-Bu), and 1173 cm^{-1} (C–O–C); NMR ($CDCl_3$) δ=1.26 (18H, s, *t*-Bu).

*Di-*t*-pentyl Ether (**2**)*: Yield, 5.56 g (35%); bp 151.5—152 °C; IR (neat) 1380, 1365 (*gem*-CH_3), and 1162 cm^{-1} (C–O–C); NMR ($CDCl_3$) δ=0.89 (6H, t, *J*=7.2 Hz, CH_2CH_3), 1.21 (12H, s, O–C–CH_3), and 1.47 (4H, q, *J*=7.4 Hz, CH_2).

*Bis(1,1-dimethylbutyl) Ether (**3**)*: Yield, 5.60 g (30%); bp 79.5—80 °C/17 Torr; mol wt, found, 187.9, calcd for $C_{12}H_{26}O$, 186.3; IR (neat) 1380, 1365 (*gem*-CH_3), and 1164 cm^{-1} (C–O–C); MS *m/e* (rel intensity), 143 (M^+−Pr, 50), 99 (79), 85 (PrC^+Me_2, 100), 59 (HOC^+Me_2, 83), and 43 (50).

*Bis(1-ethyl-1-methylpropyl) Ether (**4**)*: Yield, 2.40 g (13%); bp 78—79 °C/15 Torr; IR (neat) 1456, 1375, and 1142 cm^{-1} (C–O–C); NMR ($CDCl_3$) δ=0.85 (12H, t, *J*=7.2 Hz, CH_2CH_3), 1.20 (6H, s, O–C–CH_3), and 1.50 (8H, q, *J*=7.4 Hz, CH_2).

*Bis(1,1-dimethylpentyl) Ether (**5**)*: Yield, 6.00 g (28%); bp 109—110 °C/20 Torr; mol wt, found, 215.8, calcd for $C_{14}H_{30}O$, 214.4; IR (neat) 1380, 1364 (*gem*-CH_3), and 1161 cm^{-1} (C–O–C); MS *m/e* (rel intensity), 157 (M^+−Bu, 30), 101 (26), 99 (BuC^+Me_2, 100), 59 (HOC^+Me_2, 39), 57 (78), and 43 (16).

*Bis(1-ethyl-1-methylbutyl) Ether (**6**)*: Yield, 2.36 g (11%); bp 111—112 °C/20 Torr; mol wt, found, 214.6, calcd for $C_{14}H_{30}O$, 214.4; IR (neat) 1463, 1380, and 1145 cm^{-1} (C–O–C); MS *m/e* (rel intensity), 185 (M^+−Et, 8), 171 (M^+−Pr, 13), 101 (10), 99 (71), 87 (HOC^+PrMe, 58), 73 (45), 57 (100), and 43 (19).

*Bis(1,1-diethylpropyl) Ether (**7**)*: Yield, 0.20 g (1%); IR (neat) 1455, 1380, and 1131 cm^{-1} (C–O–C); MS *m/e* (rel intensity), 185 (M^+−Et, 31), 99 (C^+Et_3, 88), 87 (HOC^+Et_2, 100), 57 (98), 45 (29), and 29 (19).

*Bis(1,1-dimethylhexyl) Ether (**8**)*: Yield, 2.66 g (11%); bp 131—131.5 °C/16 Torr; IR (neat) 1382, 1367 (*gem*-CH_3), and 1152 cm^{-1} (C–O–C); MS *m/e* (rel intensity), 242 (M^+, 5), 171 ($M^+-C_5H_{11}$, 62), 115 (13), 113 ($C_5H_{11}C^+Me_2$, 80), 71 (66), 59 (HOC^+Me_2, 100), 57 (68), and 43 (79).

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